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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,910	02/06/2001	Robyn Joyce Russell	50179-087	3696

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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,910	RUSSELL ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-11 and 14-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23* is/are allowed.

6)☒ Claim(s) *9-11,14-22 and 24-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 9-11, 14-30 are currently pending and are present for examination. Claims 9-11, 14-30 are now under consideration.

Applicants' amendments, arguments filed on 5-31-05 in response to the previous Final Office action and the Declaration filed under Rule 1.132 filed on 2-15-05, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The finality of the previous Office action is withdrawn. A new non-final action is now in place.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 9 and 18 recite the phrase "capable of hydrolyzing". The phrase "capable of" attached to the term "hydrolyzing" conveys that there could be certain conditions required for hydrolyzing the organophosphate thus rendering the whole phrase ambiguous and the claims indefinite. Examiner suggests deletion of the above phrase and replacing it with a more direct phrase "which hydrolyzes" to remove any ambiguities.

Claims 14, 15 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 14 and 15 recite the phrase "80% identity" and "95% identity" respectively. While it appears that applicants are claiming a sequence identity, the claim as written does not bring out that aspect fully rendering the claims unclear as to what the identity is connected with. Examiner suggests amending the claim to recite "amino acid sequence identity" in order to render the claims definitive.

Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19 recites the phrase "enzyme said DNA molecule..." which renders the claim unclear. It is not clear to the Examiner whether applicants are claiming a DNA or a protein. Correction is required.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 29 recites the phrase "as provided in SEQ ID NO:10" and "as provided in SEQ ID NO:13". It is not clear to the Examiner as to what applicants mean by the phrase "as provided in". It is not clear whether the claimed sequence comprises or consists of said SEQ ID NOs. Examiner suggests referring to the sequences directly by their SEQ ID NO: such as "encoding a recombinant enzyme having an amino acid sequence, SEQ ID NO:10".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-11, 14-17, 19-22, 24-28, 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant enzyme which hydrolyzes at leadt one organophosphate comprising an amino acid sequence SEQ ID NO:8, 10 or 13 and encoded by the polynucleotide with SEQ ID NO:1, 3, or 5 with the proviso that Trp at position 251 is replaced with amino acids Leu, Ser, Ala, Ile, Val, Thr, Cys, Met or Gly and a method of eliminating or reducing the concentration of organophosphate pesticide residues in a contaminated sample comprising contacting the sample with an enzyme having an amino acid sequence SEQ ID NO:8, 10 or 13 encoded by either SEQ ID NO:1, 3, or 5 and having a amino acid substitution at position 251, wherein the substituted amino acids are either Leu, Ser, Ala, Ile, Val, Thr, Cys, Met or Gly and capable of hydrolyzing organophosphates, does not reasonably provide enablement for a recombinant enzyme comprising an amino acid sequence that is at least about 60%, 75%, 80% or 95% identical to SEQ ID NO:8, 10 or 13 and encoded by SEQ ID NO:1, 3 or 5 or polynucleotides which hybridize under stringent conditions to SEQ ID NO:1, 3, or 5 or such a method in which any of the above said enzymes are used. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3)

the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 9-11, 14-17, 19-22, 24-28, 30 are so broad as to encompass any recombinant enzyme comprising an amino acid sequence that is at least about 60%, 75%, 80% or 95% identical to SEQ ID NO:8, 10 or 13 and encoded by SEQ ID NO:1, 3 or 5 or polynucleotides which hybridize under stringent conditions to SEQ ID NO:1, 3, or 5 or a method of using such enzymes degrading organophosphates wherein the encoded enzyme has an amino acid substitution at position 251, wherein the substituted amino acids are either Leu, Ser, Ala, Ile, Val, Thr, Cys, Met or Gly. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of said enzymes broadly encompassed by the claims including variants, mutants and recombinants. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one said enzyme comprising the specific amino acid changes mentioned above. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching making and using amino acid sequence encoded by SEQ ID NO:1, 3, or 5 wherein said encoded sequence differs from SEQ ID

NO:8, 10 or 13 in having an amino acid substitution at position 251, wherein the substituted amino acids are either Leu, Ser, Ala, Ile, Val, Thr, Cys, Met or Gly and wherein said polypeptide continues to have organophosphate hydrolyzing activity but provides no guidance with regard to the making of variants and mutants for use in the methods as claimed. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompasses polypeptides and polynucleotides comprising broad modifications to their sequences and the use of said polypeptides to degrade organophosphate, because the specification does not establish: (A) regions of the protein structure (except for the amino acid position 251 which may be

modified without effecting activity to arrive at either 60%, 75%, 80%, 90% or 95% amino acid sequence identity to SEQ ID NO:8, 10, or 13; (B) the general tolerance of above enzymes to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues in the above polypeptides with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices of all those polynucleotides which hybridize to SEQ ID NO:1, 3, or 5 are likely to be successful in encoding said polypeptide.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including enzymes encoded by encoded by SEQ ID NO:1, 3, or 5 polynucleotides including variants, mutants and recombinants. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of enzymes having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 9-11, 14-17, 19-22, 24-28, 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9-11, 14-17, 19-22, 24-28, 30 are directed to polypeptides which degrade organophosphates and method of eliminating or reducing the concentration of organophosphate pesticide residues in a contaminated sample comprising contacting the sample with above polypeptides including those having an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence having at least 60%, 75%, 80% or 95% identity with SEQ ID NO:8, 10 or 13 or polypeptide encoded by SEQ ID NO:1, 3, or 5 or by polynucleotides that hybridize to SEQ ID NO:1, 3, or 5. Claims 9-11, 14-17, 19-22, 24-28, 30 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue and encoded by polynucleotides that have not been disclosed in the specification. No description has also been provided of all the polynucleotides which encode the polypeptide sequences encompassed by the claim. No information, beyond the characterization of polynucleotides SEQ ID NO:1, 3, and 5 encoding polypeptides with SEQ ID NO:8, 10, or 13 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure of all the polynucleotide sequences encoding polypeptides including the claimed mutants, variants and recombinants within the scope of the genus required for the claimed method. The genus of polypeptides and polynucleotides for use in the claimed method is a large variable genus which can have a wide variety of structures. Therefore many structurally unrelated polynucleotides and polypeptides are encompassed for use within the scope of these claims. The specification discloses only three species of the genus of polynucleotides encoding three polypeptides for use in claimed method without any evidence

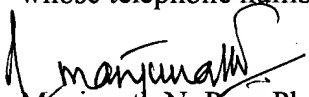
that these are representative of the whole genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Conclusion

Claim 23 is allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306/9307 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

July 6, 2005